## REMARKS

The pending claims are, Claims 241-242, 244-245. 248-250, 252-253, 256 and 265-370.

**Rejection of Claims 309-316 under 35 U.S.C. 112, first paragraph (Paragraph 8 of the Office Action)**

These claims have been rejected on the grounds that they introduce new matter. The Examiner states that the use of binding agents in detecting epitopes is not set forth in the claims. Applicant notes the final paragraph of Claim 309:

"wherein the first binding agent binds to an epitope shared by thrombospondin and the thrombospondin fragment or fragments, and wherein the second binding agent binds to an epitope present in thrombospondin but not present in the fragment or fragments".

Accordingly, Claim 309 does state that binding agents are used in detecting epitopes. Claims 310-316 depend directly or indirectly on Claim 309. In view of the forgoing, the rejection is traversed.

**Rejection of Claims 241, 242, 244, 245, 248-253, 256 and 265-370 under 35 U.S.C. 112, second paragraph (Paragraph 10 of the Office Action)**

The Examiner has rejected Claims 241, 242, 244, 245, 248-253, 256 and 265-370 as being vague and indefinite because there is no comparison step explicitly listed in the claims clarifying what level the individual's plasma level should be greater than. In response, Applicant

has amended independent claims 241, 249, 276, 289, 297 and 303 to incorporate language from their next-numbered dependent claims (242, 250, 277, 290, 298 and 304 respectively). The incorporated language makes it explicit that a diagnosis of neoplastic disease requires a comparison to a person who is not considered to have a neoplastic disease.

The remaining independent claim, Claim 309, which involves two binding agents, was also amended to make it explicit that a diagnosis of neoplastic disease requires a comparison to a person who is not considered to have a neoplastic disease.

**Rejection of Claims 241, 245 248, 249, 253, 256 and 265-276 under 35 U.S.C. 102(b) as being anticipated by Jackowski et al./ U.S. Patent Application number 2003/0119074 (Paragraph 12 of the Office Action)**

This rejection is traversed on the grounds that Jackowski does not disclose an assay directed at the diagnosis of neoplastic disease, as specified in Applicant's claims. Rather Jackowski's disclosure is directed at Alzheimer's Disease.

Although the foregoing grounds should be sufficient for overcoming the rejection, a second and also sufficient grounds exists. Independent Claims 241, 249, 276, 289, 297 and 303 now include a step (2) where the plasma level of a second individual, considered to not have neoplastic disease is measured. Jackowski (which relates to Alzheimer's disease) does not disclose or suggest that an individual considered to not have neoplastic disease be the basis for comparison.

The Examiner has discounted Applicant's argument that Jackowski has not disclosed an assay directed at neoplastic disease by asserting that: "Remiss from the claims are the patient population measured and the populations the plasma levels are compared to." Applicant respectfully suggests that assertion can not be the basis for a rejection under 35 U.S.C. 102(b). This can be seen from Paragraph 11 of the Office Action, where 35 U.S.C. 102(b) is set forth by the Examiner. As a result, there is nothing on the record that would justify ignoring the fact that Applicant's claims are directed at neoplastic disease.

Applicant respectfully requests that the Examiner indicate what section of 35 U.S.C. (or what judicial opinion) justifies the rejection.

Applicant notes that the second part of the basis for the rejection, that the populations the plasma levels are compared to are absent from the claims, has been responded to by amendments to the claims as discussed above. Applicant also notes (and believes that this was recognized by the Examiner) that dependent Claims 317-362 include, or refer to claims including, language where the method is limited to persons suspected of having, or known to have, neoplastic disease.

**Rejection of Claims 241, 242, 244, 245 248-250, 252, 253, 256 and 256-316 under 35 U.S.C. 102(e) as being anticipated by U.S. Patent Application number 2003/0166017 (McCarthy) (Paragraph 13 of the Office Action)**

This rejection is traversed on the grounds that McCarthy does not disclose an assay directed at the diagnosis of neoplastic disease, as specified in Applicant's claims. Rather

McCarthy's disclosure is directed at cardiovascular disease.

Although the foregoing grounds should be sufficient for overcoming the rejection, a second and also sufficient grounds exists. Independent Claims 241, 249, 276, 289, 297, and 303 now include a step (2) where the plasma level of a second individual, considered to not have neoplastic disease is measured. (See also steps (4) and (5) of Claim 309). McCarthy (which relates to cardiovascular disease) does not disclose or suggest that an individual considered to not have neoplastic disease be the basis for comparison.

The Examiner has discounted Applicant's argument that McCarthy has not disclosed an assay directed at neoplastic disease by asserting that: "Remiss from the claims are the patient population measured and the populations the plasma levels are compared to." Applicant respectfully suggests that assertion can not be the basis for a rejection under 35 U.S.C. 102(e). This can be seen from Paragraph 11 of the Office Action, where 35 U.S.C. 102(e) is set forth by the Examiner. As a result, there is nothing on the record that would justify ignoring the fact that Applicant's claims are directed at neoplastic disease.

Applicant respectfully requests that the Examiner indicate what section of 35 U.S.C. (or what judicial opinion) justifies the rejection.

Applicant further notes that the second part of the basis for the rejection, that the populations the plasma levels are compared to are absent from the claims, has been responded to by amendments to the claims as discussed above. Applicant also notes (and believes that this was recognized by the Examiner) that dependent Claims 317-362 include, or refer to claims including, language where the method is limited to persons suspected of having, or known to

have, neoplastic disease.

Applicant further notes that Claims 309-316 refer to methods in which two binding agents are used – one specific for thrombospondin and one specific for thrombospondin and its fragment(s) – such that the results can be used to calculate the amount of the fragment(s). Such a method has neither been disclosed nor suggested by McCarthy.

**Rejection of Claims 241, 242, 245 248-250 , 252, 253, and 256-316 under 35 U.S.C. 103(a) as being unpatentable over WO 98/07035 and further in view of McCarthy/U.S. Patent Application number 2003/0166017 (Paragraph 15 of the Office Action)**

This rejection is traversed on the grounds that neither WO 98/07035 nor McCarthy discloses an assay directed at the diagnosis of neoplastic disease, as specified in Applicant's claims. Rather the WO98/07035 disclosure is directed at arthritis and McCarthy's disclosure is directed at cardiovascular disease.

Although the foregoing grounds should be sufficient for overcoming the rejection, a second and also sufficient grounds exists. Independent Claims 241, 249, 276, 289, 297, and 303 now include a step (2) where the plasma level of a second individual, considered to not have neoplastic disease is measured. (See also steps (4) and (5) of Claim 309). Neither McCarthy (which relates to cardiovascular disease) nor WO 98/07035 (which relates to arthritis) disclose or suggest that an individual considered to not have neoplastic disease be the basis for comparison.

The Examiner has discounted Applicant's argument that neither WO 98/07035 nor McCarthy has disclosed an assay directed at neoplastic disease by asserting that: "Remiss from the claims are the patient population measured and the populations the plasma levels are compared to." Applicant respectfully suggests that assertion can not be the basis for a rejection under 35 U.S.C. 103(a). This can be seen from Paragraph 14 of the Office Action, where 35 U.S.C. 103(a) is set forth by the Examiner. As a result, there is nothing on the record that would justify ignoring the fact that Applicant's claims are directed at neoplastic disease.

Applicant respectfully requests that the Examiner indicate what section of 35 U.S.C. (or what judicial opinion) justifies the rejection.

Applicant further notes that the second part of the basis for the rejection, that the populations the plasma levels are compared to is absent from the claims, has been responded to by amendments to the claims as discussed above. Applicant also notes (and believes that this was recognized by the Examiner) that dependent Claims 317-362 include, or refer to claims including, language where the method is limited to persons suspected of having, or known to have, neoplastic disease.

Applicant notes that Claims 309-316 refer to methods in which two binding agents are used – one specific for thrombospondin and one specific for thrombospondin and its fragment(s) – such that the results can be used to calculate the amount of the fragment(s). Such a method has neither been disclosed nor suggested by either WO 98/07035 or McCarthy.

**Provisional rejection of claims as being unpatentable over claims of copending application No. 10/525,610 on the grounds of nonstatutory obviousness-type double patenting (Paragraphs 16 and 17 of the Office Action)**

Application serial No. 10/525,610 was expressly abandoned on April 7, 2010, the Notice of Abandonment being issued on April 9, 2010.

On February 26, 2010 Applicant filed application serial No. 12/713,952, which is a continuation of application serial No. 10/525,610. (Application serial No. 12/713,952 is referred to below as "the '952 continuation.") A preliminary amendment of February 26, 2010, was filed in the '952 continuation on February 26, 2010 amending the claims in that application. On the chance that the Examiner may wish to pursue this provisional rejection in the context of the '952 application, Applicant responds further as follows:

The Examiner states: "A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claims(s) because the examined application claim is either anticipated by, or would have been obvious over the reference claim(s)." (Paragraph 16 of the Office Action; *emphasis by underlining added here*)

Application Ser. No. 10/525,610 had the *reference claims* in the context of this rejection. The claims to kits in in the '952 continuation (should the Examiner elect to make its claims *the reference claims)* as amended on February 26, 2010, do not specify that the kits are to be used for the diagnosis of neoplastic disease. In contrast, the claims to methods in the present case, Application serial No. 10/782,968, *the examined application claims,* do specify that methods are

directed at the diagnosis of neoplastic disease. Therefore the claims to the kits in the '952 continuation neither anticipate nor make obvious the method claims in the present application.

Accordingly this rejection is traversed.

Should the Examiner believe that a telephone conversation would be useful, Applicant's undersigned attorney can be reached at **610-724-2952**.

Respectfully submitted,

CAESAR, RIVISE, BERNSTEIN,
COHEN & POKOTILOW, LTD.

May 6, 2010

By Allan H. Fried

Allan H. Fried
Registration No. 31,253
Customer No. 03000
(215) 567-2010
Attorneys for Applicant

Please charge or credit our Account No. 03-0075 as necessary to effect entry and/or ensure consideration of this submission.